

Activation of the Human Thrombopoietin Gene by Homologous Recombination: Embodiment 1

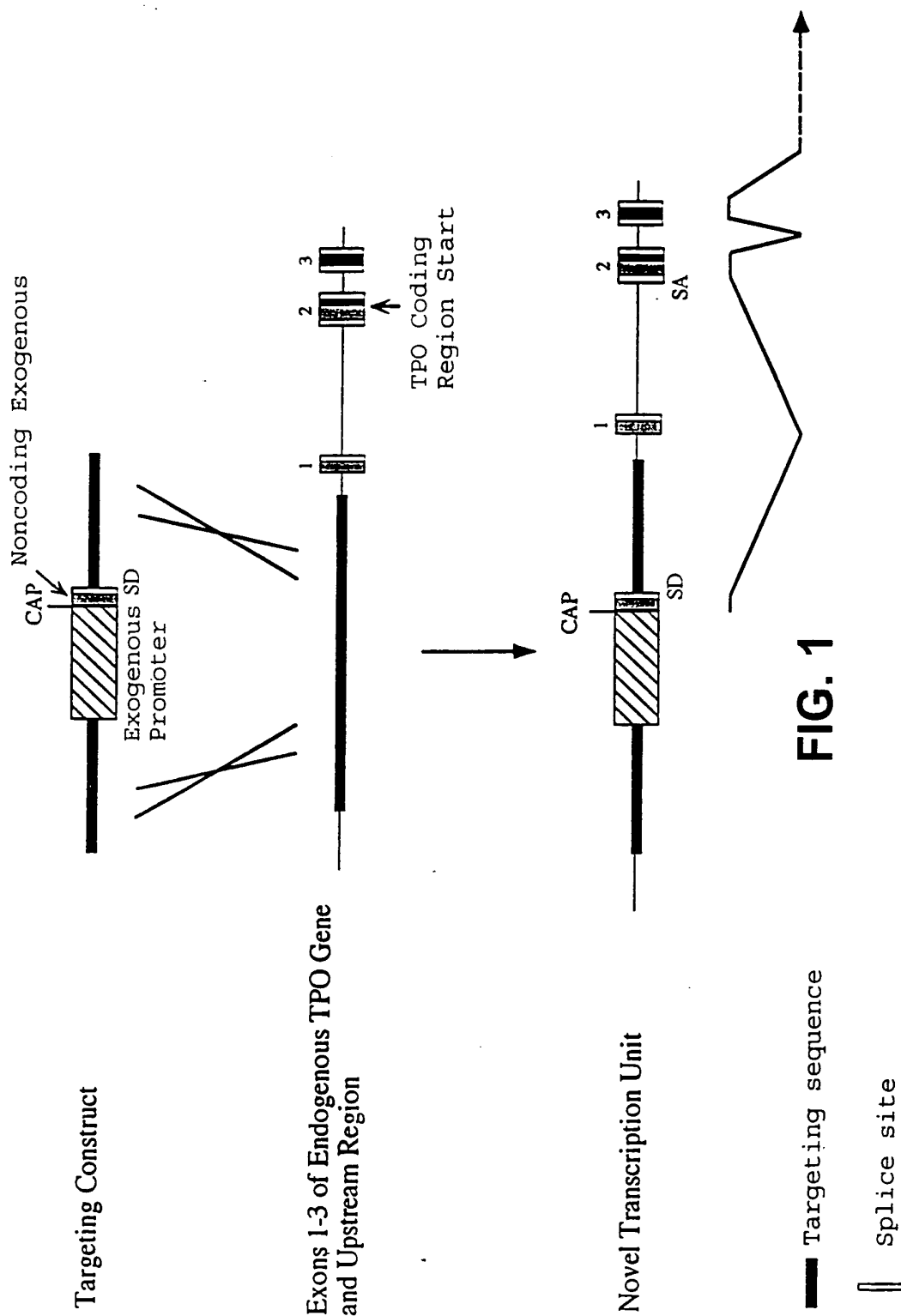


FIG. 1

Activation of the Human Thrombopoietin Gene by Homologous Recombination: Embodiment 2

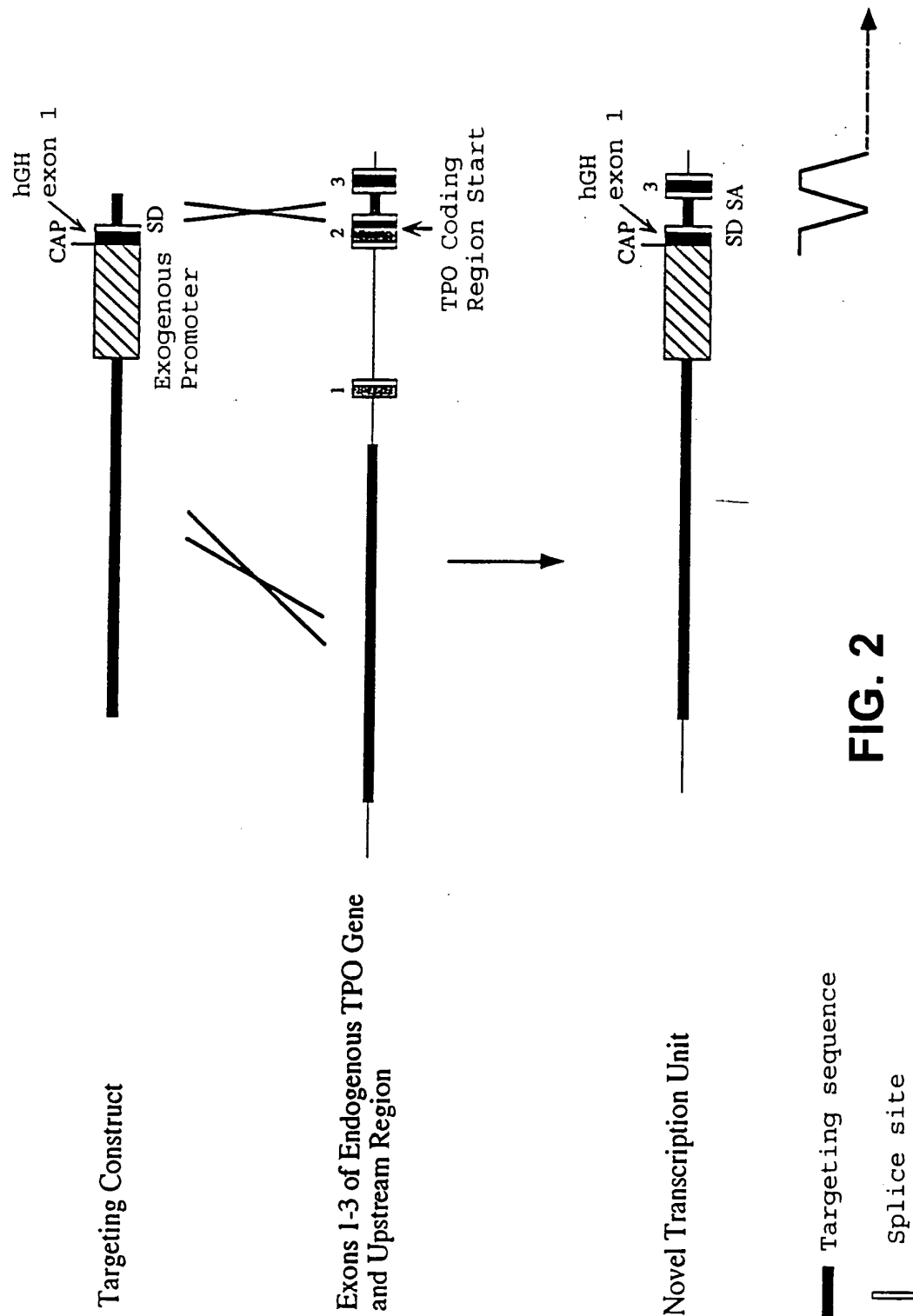


FIG. 2

669070 BT 652260

HUMAN THROMBOPOIETIN

5' Flanking sequence and Exons
1, 2 and 3

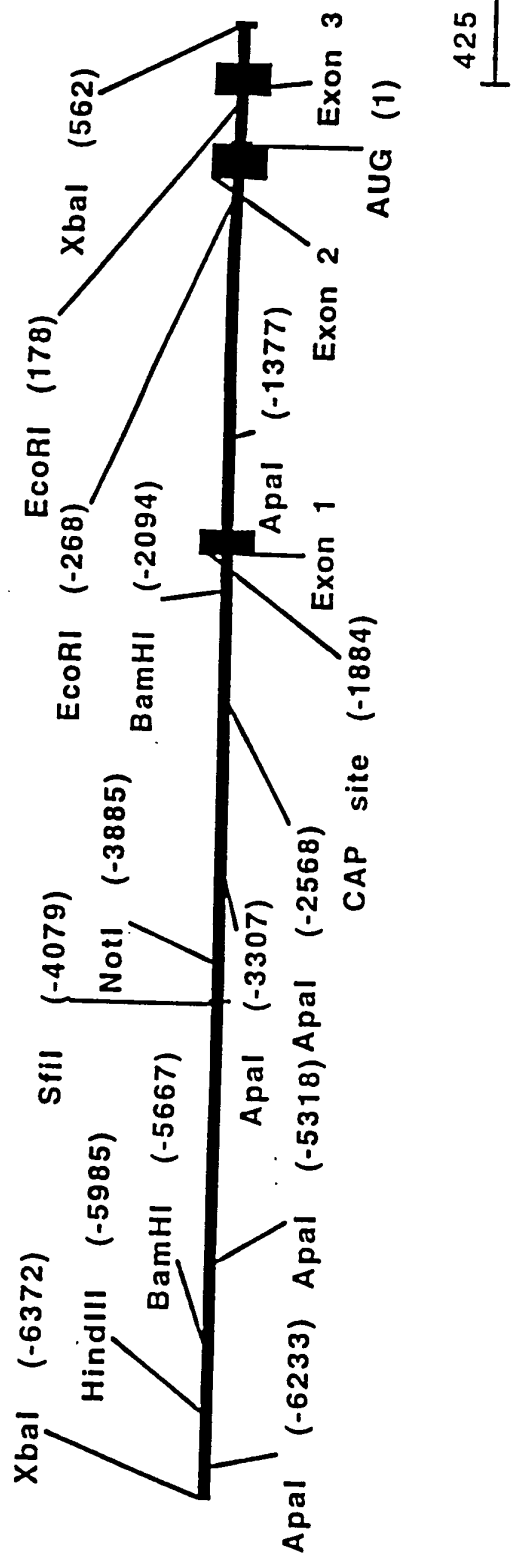


FIG. 3

XbaI (-6372)

-6373 TCTAGAGTCAGGATGGCACTGAAGGTCTCTGGGGAAGGGACGATGATGAGAGCCCGTCAGAA
-6311 ACCCTCCCCCTTTCTGGGTGATAGAGAAGACTCAGAACTTCACGCCCCGGGCTCTTTGCT

Apal (-6233)

-6249 CCCTACCTGCAGCCAGGGCCCGGTGCGATGAGAGCCCCCAGACCTCCCTGAAGGGTGAGTGA
-6187 GTGTCACAAGTGCCACATGCAGCTGTTCTGCCCTAAGGAGCCGCAGAGACAACCGAGGCACT
-6125 GCCCCCCACACCCACAGACCTGGAGCAGAGAGACAAGAAGGCCCTACGCTCAGACACTGTG
-6063 CAGGCTAGGCCAATTAGGATGCCCAGGCAGGGCTTATGAAAAAGGAACATGGAAAGGAACCT

HindIII (-5985)

-6001 CCAGGGTGCCCTAGGAAGCTTAAGAAAGAACGCTGGAGCCAGATGCTTGGGTTCCAATCCTG
-5939 GCTGCACCACTTCCTAGCTGTGTGACCTTGAATCAAATCACATTATCCTACTGAGCCTCAGT
-5877 TCCCCCTTCTGTAAAAATGGGCATCATAATGTCAGTGCCTTCTCCCACTGGGCTGTGGTGAG
-5815 GACCACGGGAGGCAATGCAGAGCATGCTCTCGGCACAGTGCCCACTGGGCAAGTGCTATA
-5753 AATGGCATCATCTCACCAGGCCTATCTTGGGTTGRGTGGGCTGCAGGGTGCTCAAACAGGAC

BamHI (-5667)

-5691 ACTGCCATTGGAGTCTGAGAAGCGGATCCTGGTAGGGCGGTCCAGCCTGGGAATGAGAGGTC
-5629 GGGTGAGGCCGGACTGAGCCAAAAGCAGCCCCCTCCAGCTCTCCAGTTTCCCTCCSGGCCC
-5567 CGGCAGCGTGACCCCTCCTTGCTCCTTCCCCCTTCTCAACGCCTGTAGGAGATAGAGAAGCG
-5505 GAGGCTAGAGCGCCAGCAGCGAGACTCGGCTCGTGCCACCGCCTGCGACCTCGGCCCTGTCA
-5443 GCAGCGCCACGAAGTCTGGGACGGGAGGAAGATGGCCTGAGCACTGTCAAACGCCGCTTTGG
-5381 TGGCCCAGCCTCAACCACAACCCCGCTGTTGCGCCAGCCCCCTACCCGTGTGGCCGTCAACCAC

Apal (-5318)

-5319 GGGCCCGCTCCTCAGCGCCTGGCTCCCCGCGGTGCTATAACTGCGATGCTCCGGGTCCCGC
-5257 GGATACACGAAGGACAGGCCGCTCGGCTGCCGCTCCGAAGTCTGCGCTCTGCGGSGGGGGG
-5195 GTAAGAACACGGGCTTCAGCTGGCCATGGGAAAGGCCAGTCCGACGCCCCATCCAAGTGGCC

FIG. 4A

-5133 CGGGACCTAGTATCGTGGCCCTGCCTCCCTCCCCGCAGCGGAGCAAGACTTACCCTGGGGGC

-5071 AGGTCTGGCAGCAGTGTCCCGGCAGCTGGCGCGGCTGCCCCACAGGCCGGGGTTGGGCACTCT

-5009 GGTTTGATGTTCTTGCAGCTGACCCTGCCAGGCCCTGGTACGGCGACCCCACTGAGGCTGC

-4947 TCCCGGAAAAGGCGGGAAACCCAAGTGAGTGCAAGATGCCAACTGATGAGACCCCCCAGGC

-4885 AAGGATGTCCCGCAGAGTCAGCCAGCTCTGCCACTTACAAGCTGCGTGACCCTAGACAAGCT

-4823 ACTTCATCTCTCTGGGCCTCAAGGTCCCTGTCTGGAAAATGGGGATAATAATACTCTCTATC

-4761 TAGCAAGGCTGCCATGAGAGTTAGATGAGCAGGGAACGAAACGGAGTTGGCACAGAGCCTCA

-4699 CACAGAGTGGGCGATCAGTAACAGCACCTAAGAATTGGAGGGGCTGATTCCCCCTTCTCCAC

-4637 CAGAAAAATATCCCCAACATCTGCCGACTGGGCTCCTTCTCAGCAGCTCCGAGTCCACTCCG

-4575 ACGCCCGCGCGACCCGGCCGTCCCCACCCGCCAGCCCGGGCCGGCCGCGGGGTGCACTCACC

-4513 GCCTCGCAGGCCACAGCACGCAGCGCATCACCCGAATGGCTCCCCCTAGGTCCGGGTGCCAC

-4451 GTCTCGTCCAAGGCATAGACCTTCCCGCCGAAGTGCAGCCTGCGGGACGGGCTTGGCTGGAG

-4389 GCGCTGCCCAGCTCGCGCCGTGTGCCGCCCCGGGGGCTGCCCGCGGGTCCCCGGTCCCAGGC

-4327 ACCGCGCCCTTCTGCCCCCGCCACCCCTCCGGGCGCCCGCCGCGCCGAGCCACCTGCGCCC

-4265 CGCGCCCCCTCCTCCGGCTCGGCTGACTCGCCCCGAGCCCGACTCCCCGCCCCCTCCCCCGG

-4203 GCGCCACCTACCCTGCTGCCCCAACGGGCAGCGGCTCCTTCTCAGAACGGATGGGCAGCAC

Sfil (-4079)

-4141 GGGGGCTCTCGGGCCGCGCGGGGCGGGAGCCGAGCAGCAGCAGCCCGAGGAGCAGCAGCGGG

-4079 GCCGGCGGGGCCGGGAGGGCHCGGCATGACGCGAACGGGACAGCTGGGGAGGAGGGAGGGAG

-4017 GAGGGCGCGGGAGCGGGCGGAGGGAGGGAGGGCGGGAGTGCGGAGGGCGGAGGGCCGGGCCGG

-3955 GGGCGGTGCGGCGGGAGGGGGCCGGGGCCGGGGCCGGGGCCGGGGCAGTGCCCGCGAGGGGC

FIG. 4B

[illegible]

FIG. 4C

003049-04000

-2653 GACAGGGACACATGGGCCTGGTTATTCTCTTGTACATGTGGAACGGTAGGAGATGGAAGA

Apal (-2568)

-2591 CGGAGACAGAACAAGCAAAGGAGGGCCCTGGGCACAGAGGTCTGTGTGTGTAGCCATCTAAG

-2529 CCACTGGACCCCAGCAGACGAGCACCTAAGCTCAGGCTTAACCAGTGCACGTGTGCGCACAT

-2467 ACTGTGCCCCGCACCTGACGTCCACTCAACCCGTCCAAACCCCTTCCCCATAACACCAACCC

-2405 ATAACAGGAGATTTCTCTCATGTGGGCAATATCCGTGTTCCCACTTCGAAAGGGGGAATGAC

-2343 AAGATAGGACTCCCTAGGGGATTACAGAAAGAAAAGCAGGAAAGCAAGCATCCTGTTGGATT

-2281 TCAGCAGCAGGTATGATGTCCAGGGAAAAGAAATTTGGATAGCCAGGGAGTGAAAACCCAC

-2219 CAATCTTAAACAAGACCTCTGTGCTTCTTCCCCAGCAACACAAATGTCCTGCCAGATTCTCTC

-2157 CTGGAAAAAATTCTGCTCCTGTCCCCCTCCAGGTCCAGGTTGCCCATGTCCAGGAAAAGAT

BamHI (-2094)

-2095 GGATCCCCCTCATCCAAATCTTCTCCGTGTGTGCTGTGGGTGGAGTGAGTRGWARCCCTGGT

-2033 CCAGGCAGGGVGCTCCAGGGAAGAGCAAGGCGTCACTTCCGGGSGCCTTCACCAAGTGTCTGG

-1971 TGGCTCCCTTCTCTGATTGGGCAGAAGTGGCCCAGGCAGAGCGTATGACCTGCTGCTGTGGA

-1909 GGGGCTGTGCCCCACCGCCACATG

FIG. 4D

Activation of the Human Thrombopoietin Gene by Homologous Recombination with pRTPO1

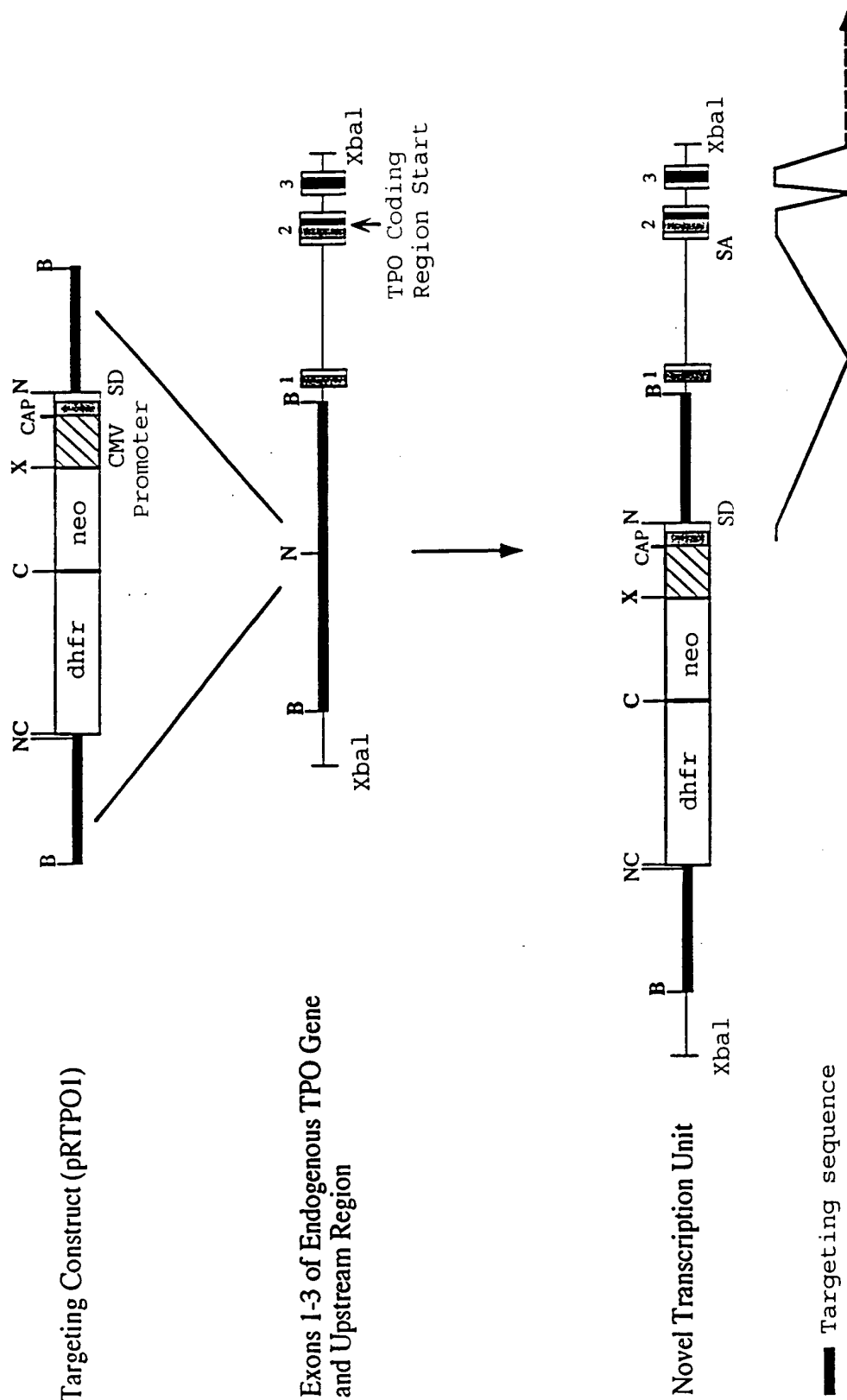
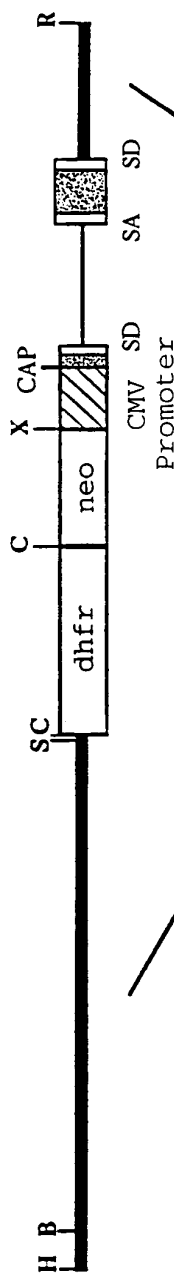


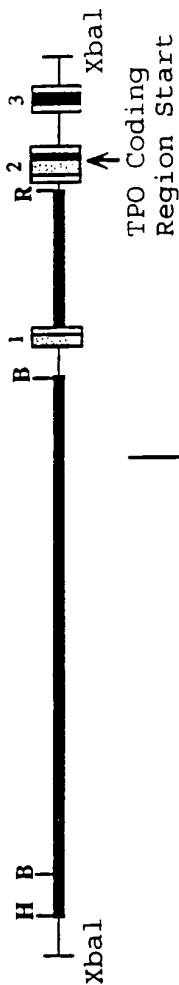
FIG. 6

Activation of the Human Thrombopoietin Gene by Homologous Recombination with pRTPO2

Targeting Construct (pRTPO2)



Exons 1-3 of Endogenous TPO Gene and Upstream Region



Novel Transcription Unit

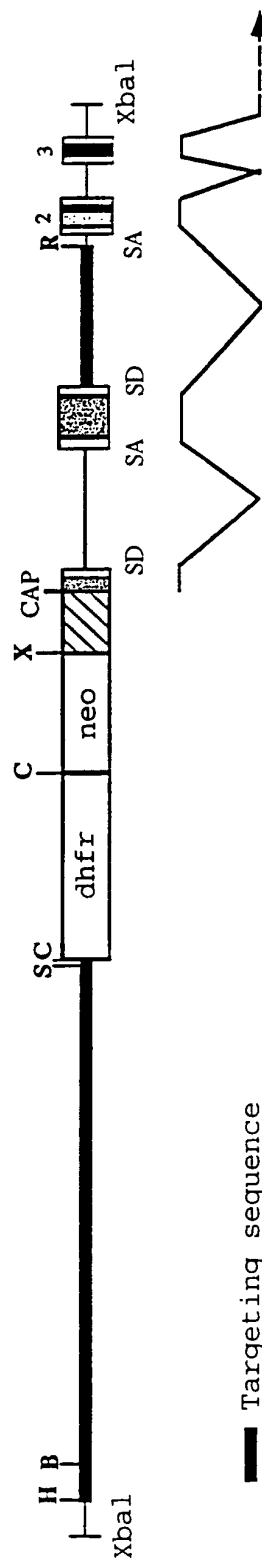
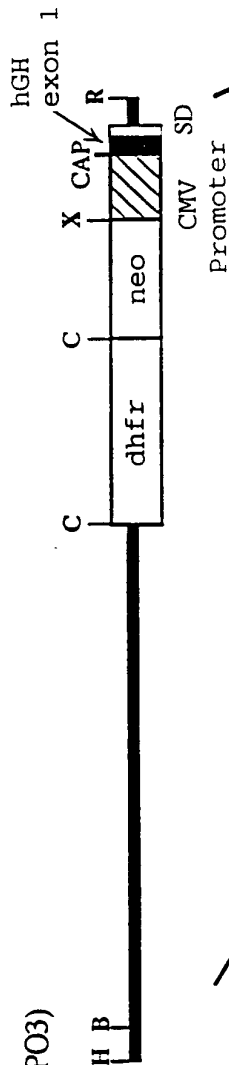


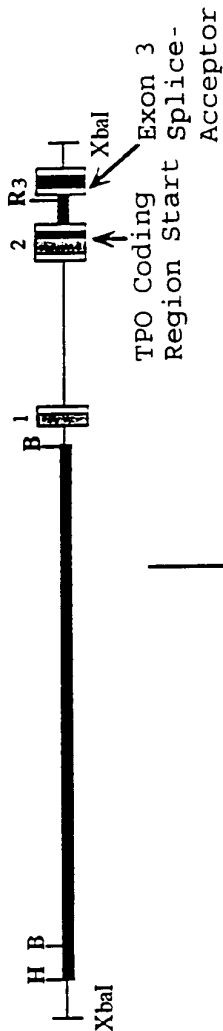
FIG. 7

Activation of the Human Thrombopoietin Gene by Homologous Recombination with pRTPO3

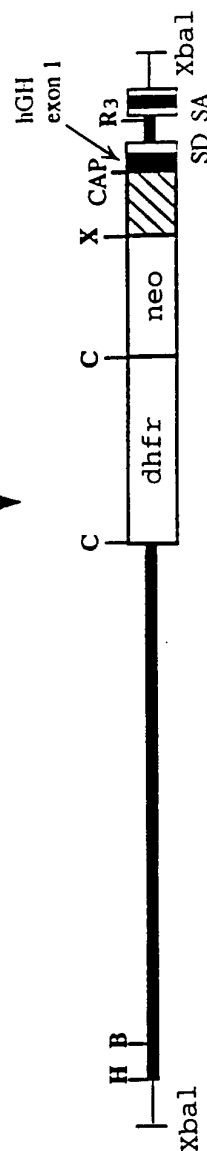
Targeting Construct (pRTPO3)



Exons 1-3 of Endogenous TPO Gene and Upstream Region



Novel Transcription Unit



Targeting sequence

Splice site

=1kb

FIG. 8

Restriction Map of the DNase I 5' Flanking Region Including Exons 1 and 2

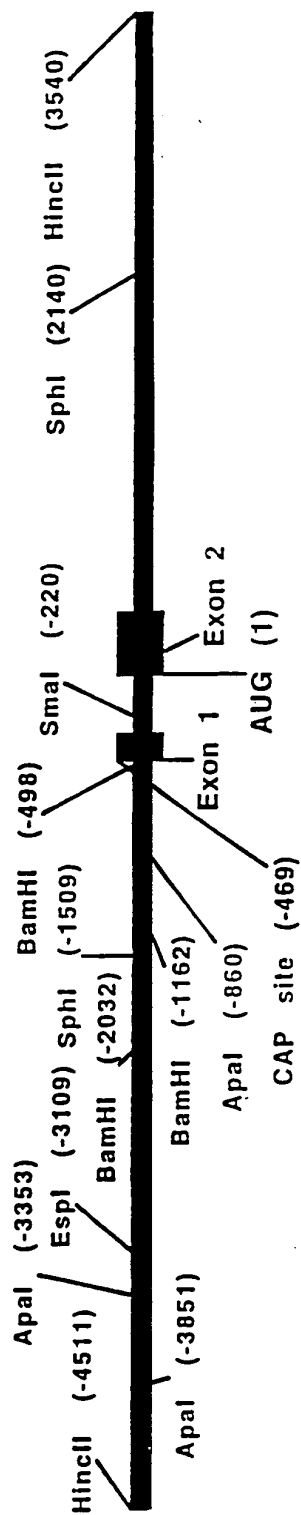


FIG. 9

[illegible]

FIG. 10A

-3232 TCCTTCTGGCAGGTAGAGGAAGCAGGGGCACTATGCCTGGGAGTTCCTGAAAGCAGATGGGGCA

-3168 GCATTTGGTCAAGAGCCAGGAGGGGATGACAGACCAGAGGGGAACCTCGTCCCACGTGCTGAG Espi (-3109)

-3104 CACACGTAGGGGGTTGGGCACTTGCTCTGTGAGCTATAATTGGTGTCCCTGTGCCCCGCCGAA

-3040 GCTGCACCAGGCAGTTTCTTGGTGGAGGACAGTGGCCGCCCTCTAGCTTTACTCCCTTCCCCGT

-2976 GATGGGTCGCTGTCAGATGTGTGTCCAGGAAAGGCAAACACCAAAGGCAGAGGACTAGTCCCTA

-2912 CACCGAATACTCCGGTGGCCTTGCTTGGGGGCTGGGTTTTGACGTGCTGGAGGCTGTCCTAGAC

-2848 TTAGAGATTAAAAACAGGAAGAACCATTGCTGAAACCTTTGGAAAAGCCTGCAATGGCCTCTG

-2784 GCAGCCTGAGGAGTGGTGGTGTTCATCTGGTAGACGCCGTCTCAATAGGAGGGACAGATGAG

-2720 TGCACCAGTGCTGCCAGCCAGAGGCGTCTGTTGGCGTGTCTTTATGGAATGGGGTGCCAGTCTT

-2656 GTGGAGGGTGGTTTTACCTTCCTGTTTCTAGTCCCCACTGGGCCTGCCTTCTGCTTCATGCCAGC

-2592 TGGCCAGACCGAGCACTTTCCTGACTTTCGACCTTGGCCCCCTGCTGACTCTTGCCGTTGAGGCC

-2528 TCCTGCAGACCCCATTTGTATTCACTTCCTGCAGTTCTCATACCTGAATCCCGCCTGGACTTCT

-2464 GCCAACCGTTCCAGGCCCTCCTCCCAGGGGACCACAGATGCTACGTGCAGGGCTGTCCTTGA

-2400 GGGCCAGCACAGCCCCTTCCAAGTGGGCAAGACCCAGGGGTGGCTCAAAAGATAGCTGTGCCCT

-2336 AGCCCTGGAACCTCTGAATGTTGATTTTTGTAGCAAAAAGGACTTGCAGATGTGAGTAAAGGC

-2272 TGTTGAGATAAGGACATCCTCCCTGCTCTCTGGGAGGACCCCAATGCAGGTGCACAGATCTTA

-2208 AGAAGAAGAGGCAGAGACTGGGGTGATGCAGCCACAATAAGGAAAGCCAAGGATTGCTGGCAG

-2144 CCTGCAGAAACTGGAGGGCAAGGAGCATCCCCCAACGCCCCGAGCCTCCAGGAGGCGCAAGGT

-2080 CCTACTGACTCCCTGACTTCAGACGTCCAGTCTCCGGAATTTTGAGAGGATCCATTTCTGTTAT BamHI (-2032)

-2016 TTTAAGCAACCAAACCTGTGGTAGTTTCACCAGTCTCAGGAAATGAATACGAATGGAAAGTCAA

FIG. 10B

-1952 AGATTCCAAGAAATGAGTGGCGGGGTGCGGTGGCTCACACTTGTAAATCCCAGCATTGCGGGAA

-1888 GATTGCTTGGGCTCAGGACTTGGAGACCTTGTGTCTGTGAGAACTTAAAAAATAGGCTGGGTG

-1824 CGATCGTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCAGGCGGATCACAAGGTCACGA

-1760 GTTTGAGACCAGTGTGACCAACATGGTGAAACCCTGTCTCTACTAAAAATACAAAATTAGCCG

-1696 GGTGTGGTGGTGCCTGTAATCCCAGCTACTCGGGAGGCTGAGGCAGAAGAATTGCTTGAA

-1632 CCCAGGAAGCAGAGGTTGCAGTGAGCCGAGATAGTATTACTGCACTCCAGGCTGGGCAGCAGAG

SphI (-1509)

-1568 CAAGATTCCGCCTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAACTGAGCATGGTAGCATGC

-1504 ACCTGTGGTCTCTCGTACGCCGGAGGATTGCCTGAAGCCAGGAGTTCAAGACCAGTCTGGACAAA

-1440 AGAGCAAGACCCCATCTCTACCAAAAAAATTTAAAAATTAGCCAGGCATGGTGCCGTACCCATA

-1376 GTCTTAGCTACTCAGGAGGCTGAGGAGGGAGGATTATCTGAGCCTGGCGGTTGAGGCTATAATG

-1312 AGCCATGATTTGGCCACTGCACTCCAGCCTTGGCAACACAGTGTGAGACCCTGTCTCAAAAACA

-1248 ATAAAAACCCAAAACAAAAGAACCAAGAAATTACTGGACCTGAGCCTGGCCTTTAGCTGCTGCC

BamHI (-1162)

-1184 CTGCCCTKTGACTGGTCACTCGGATCCCTGGGCCTAAACACACAGCCTATTGTCTACCTCAAGA

-1120 AGGCTCCCCACTGCTTGGCTGGCAATTGGGGTGGCTTTGCAGGCCCCACCTGTCCTGGCCCCAC

-1056 GGCCTGGTGCTGCAGGCCCCCACCCTGCTTGTTCGAGCTCCCCAGCCTCCTGCAGAGTTGC

-992 CTGCACCTGATGGCGATGAATCAGGAAGGCAGGCGTGTCTGGGCCACAGAGCAGTCATGCTGT

-928 CAGCCACCAGGGGGCTCCATTTGCAACTTTGGATGTGGCTTTGGCCTCTTTGTCCAAAGTGACC

ApaI (-860)

-864 TTGGGGCCCCCAGACAAGAGACAGGGAGACTGGAGCCCAGCCCCACCCTCCCGCACATACCTGG

-800 CCCATCCCTGCCCTATCCTGGAAGATGGGGGCCACCACACGTRCAAGGGACACGGGATAGGAAC

-736 CTTTGGCCTTGTATCAGACATTTTAAACTAAGTGCAAACGTGATTATCAGGTGCAGTTTTTA

FIG. 10C

-672 CAGCAGCAAGAAACCTGTGCTTACAGAAAGAAACACGTGCTAGCAACCCACCTATGCGGAAAGCC

-607 ACACAGAGCCATTGTTTTCTGCACTCTCAGGTGACGGCTCACATTTGCCCCAGGGAAGGTCACAG

BamHI (-498)

-542 CTGCCTGAACTTTTAAAACTCCCAGACACGCACTGCCTGTGCAGGATCCGGAGCCCAGCAGCACT

-477 GCCAGGG

FIG. 10D

[illegible]

334 TCT GCG G

FIG. 11

Activation of the Human DNase I Gene by Homologous Recombination with pDNase1

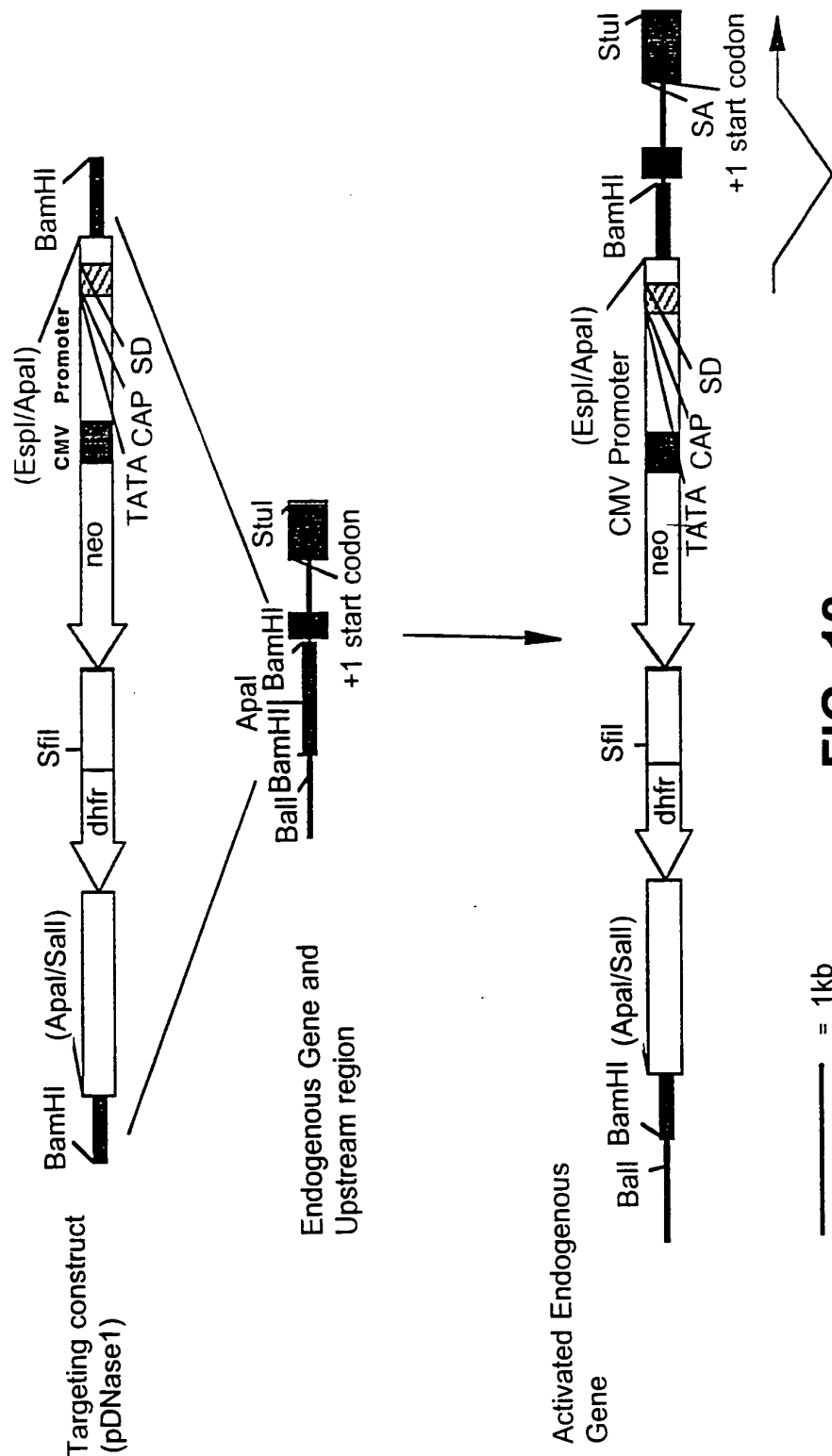
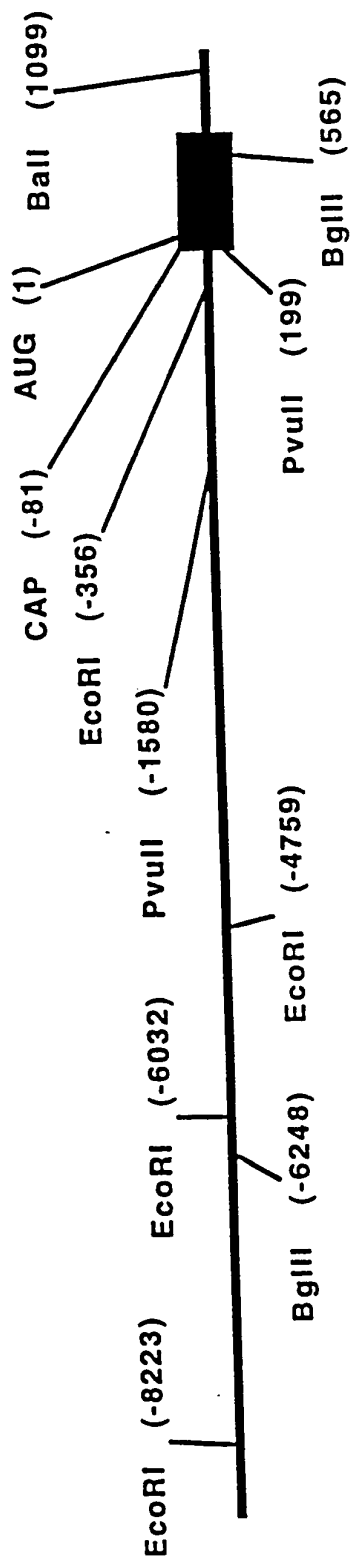


FIG. 12

Human β -Interferon

5' Flanking sequence,
coding sequence and 3'
untranslated sequence



600

FIG. 13

-8711 AGCTTCTGCTTTAGGAAAGTAGAAAAATAAGAGCAAATTAAATCCAAGGTAAGTAAAAAAAAAAAA

-8646 AAAAAAAAAAAGAAATAAAAATTAGAGCAGAAATCAATAAAATTGAAGACAGTAAATCAATAAA

-8581 GAAAATCAACATAAAAAGTCTGGTTCTTGAAAAGATATATAAAATTGATAAGCATCTACCTAGGA

-8516 TAATTAAGGAAAAAAGACAGAGGACACAGATTACTAATATCAAACATAAAAGCGGGAACATCACT

-8451 GCAAATTTTATAGGCATTGAAAGCGTAATAAAAGAATACTATAAACTATTCTATAACTACAAATT

-8386 TGATAAGTAAATAGAATGAACCAATTCCTTGAAAGACATAATCTGAAAAATGTAAAAAGAAGAAA

-8321 TAAACAATCTGAATAGCCTATATCTATTAAATAAAATTGAATCAGTAATTAATAACCTCTCAAAC

EcoRI (-8223)

-8256 AGGAAGCACAATGCCCAGATGGGTTCACTAGTGAATTCCTATCAAATATTTAAAGAAAAAAAAAATT

-8191 GTATCAACTTTCTACAATCTCTTTCAGAAGACAGAAGCAGAGGGAATACTTCCTAAATCATTCAA

-8126 CTAGGCCAGCATTACCTTAATACCGGAAGTAGAAAATGACATTACAAGAAAAGAAAACAACAGAC

-8061 CAATATCTCTCATGAACAAAGATACAAACATTTTCAACAAAATATTAGCAAAAAGAATCCAAGAA

-7996 TGTATCAAAAAATATACACCACAACCAAGTAGAATTTATTCCAGATATGTAAGGGTGGTTCAACC

-7931 TTTGAAAATCAATTAACGTAATTTGTCCCATCAACAGGTTAAAGAAGAAAATCACATGGTCATAT

-7866 TGATAGACACAGAAAAGCATTTGACAAAATTTAACACCCATTTCATGATGCAATCTCTCAGTAAA

-7801 CTAGGAATAGAGGAAAACCTCCTCAGCTTGAATGTACCTTCCTCTCAATTTTGCTATGAACCTGA

-7736 AACTCCTCTTAAAAAATAAAGTTTTTCAATTTAAAAAGAAAACAAAAACATGGAGGAGCGTTGAT

-7671 GTATCTCATTTTAGACCAATCAGCTATGGATAGTTAGGCGACAGCACAGATAGCTGCTGTACTTC

-7606 TGTTTCTGGCAATGTTCCAGACTACATTTAAAAAATTTTAAATTATAGACTTGTACTTAATGTTT

-7541 AAGAAAAATATGAAATGCTTTGCCGTGTTAATGCTACTCTTTTTTAAAAAAAACATAAGTTCAA

-7476 ACTTTATTTATATTTTCATTAGTTTTTTAGCTACTGTTCTTTTTCTGTCTGGGATCTCATTGAGA

FIG. 14A

0033719-010609

-7411 ATGCCACATTACATATAATTCTCATGTCTCCTTGGGTTCTCTTAGTTTTGACAGTTCCCTCAGAC
-7346 TTTTCTTATTTTTGATGACCTTGACAGTTTTGAGGAGTACTGGTTAGATATAGGGTAATGGTTTT
-7281 TAAAGTATATTTGTCATGATTTATACTGGGTAAGGGTTTGGGAGGAAGCCATGGGTAAGTACTGT
-7216 TCTCATCACATCATATCAAGTTATATACCATCAATATTGCCACAGATGTTACTTAGCCTTTTAAT
-7151 ATTTCTCTAATTTAGTGTATATGCAATGATAGTTCTCTGATTTCTGAGATTGAGTTTCTCATGTG
-7086 TAATGATTATTTAGAGTTTCTCTTTCATCTGTTCAAATTTTGTCTAGTTTTATTTTTTACTGATT
-7021 TGTAAGACTTCTTTTTATAATCTGCATATTACAATTCTCTTTACTGGGGGTGTTGCAAATATTTT
-6956 CTGTCATTCTATGGCCTGACTTTTCTTAATGGTTTTTTAATTTTAAAAATAAGTCTTAATATTCA
-6891 TGCAATCTAATTAACAATCTTTTCTTTGTGGTTAGGACTTTGAGTCATAAGAAATTTTTCTCTAC
-6826 ACTGAAGTCATGATGGCATGCTTCTATATTATTTTCTAAAAGATTTAAAGTTTGCCTTCTCCAT
-6761 TTAGACTTATAATTCACCTGGAATTTTTTGTGTGTATGGTATGACATATGGGTTCCCTTTTATTT
-6696 TTTACATATAAATATATTTCCCTGTTTTTCTAAAAAAGAAAAAGATCATCATTTTCCCATTGTAA
-6631 AATGCCATATTTTTTTCATAGGTCACTTACATATATCAATGGGTCTGTTTCTGAGCTCTACTCTA
-6566 TTTATCAGCCTCACTGTCTATCCCCACACATCTCATGCTTTGCTCTAAATCTTGATATTTAGTGG
-6501 AACATTCTTTCCCATTTTGTTCCTACAAGAATATTTTGTATTGTCTTTTGGGCTTCTATATACA
-6436 TTTTAGAATGAGGTGGCAAGTTAACAACAGCTTTTTTGGGGTGAACATATTGACTACAAATTT
-6371 ATGTGAAAAGAAAGTATACCTTCACAATATTAAGTCTTTTAGTTTCATGAATATAGTATGTCTCTC
-6306 CGTTTCTGCATTAACTTAGACATTCATTAATTTCTCTCACAATTTATAAGTTTATTTAGATCTTC
-6241 ATTCATTTAAATCTTCACTAACCTCTCATTTACAATTTGTAAGTTTTCTGGGTAACAGTCTTGCA
-6176 CTTCTTTGCCTAGATTTATTTCCAAGTAGATTATTTTCATACATCGTCTATGGTGTCAATTTTTAA

BgIII (-6248)

FIG. 14B

-6111 AATGTAATTTTTTACCTTTTTATTGCTAAAGAGAGATGACTGATTGTTAATATTGATCTTGTGCG

EcoRI (-6032)

-6046 TGGCGACCTTGCTGAATTCTAATCGTTTATCTATAAATTCTTTTGTATTTTGAATGTAAACAATT

-5981 AGATCATCTGCATATAATTTTTTAAATCTGATAAGTCAACAAGAGATTGAAACAGGCTCTTCACA

-5916 AAGAAAATATCCAAATGGTCAATAAACATATGAAAAGATGCTGAAACTTGTTAATAATCAGAGAG

-5851 ATGCAAATTAACTATAATGAAGTATTATTGTACAACAATAGAATGACTGAAATTAAAAAGACTG

-5786 ACAATATCAAAGTTGGCAAGAGTCTGATACAACTGGAACCTTCTCAAACACTGTTAGTAAGAATGT

-5721 AAATTGGTACAAACATTTGGGAAGTCATTACAATATTATCTGCTAAATCTGAACATATACATATT

-5656 CTATGAGCCAGTTACTTCATTCTAGGCATATACCCAAAAGAAGTATGTACTATTGTGCAGTAAAA

-5591 AATACAGACAAGGAATTTCATAGGAGCATTAAATTATCATGGCAAATATTTTAAAAAATTATTAGT

-5526 AGTAGAAGGGATAAAACATTGTGGTATACTTCTAAATAGGGTAAACACATTAATGTAAATTAAT

-5461 AACTATACACACAAGATAGACGAATTTCCGAGACATTCTGTTGAGGGTAAGAAGACCATTTATA

-5396 CAAAGCTCAAAAACAGACAGAATCTAGAGTGTTAAAAGACTGCATGGTAGTGACTTTGGGAGAAG

-5331 AAAGTAGTGACGAGAGAGAGGAGAGAGAATAATGATTGCGAGGTGCTATAGTCTGAAGGTTTGTG

-5266 TCCCCCAAATTTACATGTTAAACCTAATCCCCAATGCAATCATTTTAAGAAGTGGGTCCTTTA

-5201 GTGGATAATTAGGTAATGGAACAAGAGCCCTAACAAATGGGATTGGTGCCTTATAAAAGAAGCCT

-5136 GAGCCTGAGGGACCTTGTTTCCGCTTCTACCATATGAGAATGCAATGAGAAGGCACAAAGCAAA

-5071 GAGCAAGCCCTCATCAGACACTGAATCTGCTAGGGCCTTAGTCTTGGCTTTTCCAACCTCCAGAA

-5006 CTATAAAAAGAAATGCTTGTTGTTTAAAAGGCATTCACTCTATCGGTGTTTGTAGAGCAGCCC

-4941 CAAGAGACTTAAGAGGGAACAAGAGGGCGATTTCTGTTGTGTTGATAATGTTTAGTTTGTGGTTA

-4876 CAAAGAGTGCAGACGTTTTTATTTTATAACAATTCATTGAGCTATATCTTAAGATGTATGCGTAA

FIG. 14C

EcoRI (-4759)

-4811 TTTTCTATGTATATTATTGTTTTATAAACTTTTCTTAAAAGAGGAAATGGGAATTCTCCCTTTT
-4746 ATGTATTAATCTCTTATGAAAGAGTTTGTGGCTTCCCAAGATATTTCTGAAAGATTGCTTTTGG
-4681 CTTCAATTTATGTTCTGCCACTGCTTATGCACCTCTCAATAACTCTTCATCTTGTATAATTTATCA
-4616 TTCTTTGATAGGGACCCCTCTTCCTTGAAAAATAATTGAAGATATAAGGAGGAGGAAGAGAAGACA
-4551 ACTAAATGTTTATTTCTAGATACATAGTAGTCTGCATAGATAATTATATTCAAAGAGGAGGACA
-4486 AATTGGCTCCTATCTCTGAAATTTATAGAAAAGCATTTCACATTAAAGTGATTTCAAATGACTA
-4421 GAAATGTCATTCAAGTTTTACTTTCTAAATGTCACCTCTGTCTCTCCAAACCTCATTAAACCACAAG
-4356 GAACTGGTGCAGGGACTGGAAGTAGTTTTCTCATACAACGGAAAGTTAACGAGGGGAGGAAAGGA
-4291 TGTGTGCAAAAATAACGTCCACAGAAGGGACAAATAACAAAGGGAAAGATGACAGGAAAGGGTTC
-4226 GGGCACTAACCCTTACAATGCAGATACACACTGGGCTGGTCTAAGAAATAGGGTTCCCTGGTAGA
-4161 CAGAAGGTTAAATAAATTTTCTGGTTATTCTGATCAACTCTAATAAAAGAAGAGAAATGAAGC
-4096 TAAAACTTAAATGATGTATTTAAAGGAAGAAATTTTAACCCATTTCATAGGTGAGCTTCTGCCA
-4031 AGATTACTACTAATCCTCAGGAGAAGGGGTAGAGGAGAACTCCATAAAGGCAACTGGAAGTGGA
-3966 GTATTAGGAAGCACCTCAAGAACACAATAGCAGGAAGTAGCTAGAGAACAAGAGAAGAAAACCA
-3901 GAAAAAAAAAATCCCTTTTTATTTTTCTGTTTCCATTCTTTGGCTCCATTTCCACAGCTATGGC
-3836 CTTTATTTTACCCTCCACAGCCATGAGAGCCTCTGGGCAGGAGTTCTCTCGCCTCTCCCTGTT
-3771 CCAATCACCTCTAACATTTCTGCCTATTGTTCTGCCCAGGGAAAAAACTCCAGTCTCTTCTCTGT
-3706 CAAAGACCTCTTGAATTAAGTCCAAATGCTACACTCTGGCATTCAAGACTCGTAATACAGCTCAA
-3641 CCTGACTTTTCCACCCTCAGCCTCCTTGATTCTTAAATGAAGCCTGTCCACAATTGAAGCTCCT
-3576 TGTCTTTGCTCCTGCAAATTTGTTCAATCTCTCTGGCTGTGTTTGTGCTGGTCTCTGTCTATCTAG

FIG. 14D

-3511 AGCTGTGGATATCATGGTATCTATTGTCTATCATGCTAGCCATGAACCACATGTGGCTGGTGAGC
-3446 ATTTTATATGGTACTAGTCTAAATTGACATCTACTGTGAGTGTA AAAATGTGCATTATGTTTTGA
-3381 AGACTGTACACAAAATTTAATTATCTCATGAATAATTTTAGATTGGTTATATGTTGAAATTATAA
-3316 TATTTTGGATATACTATGCTAAATAAAACATATTATTAAATTAACCTCACCTGTTTCTTTTCCT
-3251 CTTTCAATATGGCTACTAGAGCTTTTAAATTGCATTATGTGACTTTATTGGACAGTACCGATTG
-3186 AATGCCCTCAACCACATCACCTCACCACAGCCACCTCTACCTGTAGTGATCATACCACTTCTTTA
-3121 GGCACACTGCCTGCATTAAGGGCAATGAATGCCTTTTCATCTTCTCCACTAGATGTAGTTTCTTT
-3056 TTTCTTTGAGAGCCATCATCACCATCATGGTTGACACCATGAACCTATCTGAAGATGTCAGCCAT
-2991 AGACTGCTTGATATTCTACAGGAAAGATCACAGTTTTAAGTGCAATCTACCCATGTTATTAGCAG
-2926 TGTGTATCTTTACACATTACACAGCCTCTCTAAGCCTCATTTCTCTCCTCTGTAAGATGGGGAT
-2861 GATAATAACCCATCTCAAATGTTTTACTATGAGGATTATTCAAAGAATGGCAAATAGCAAGTGCTT
-2796 AATAAATGATAACTAGTACTACCGCCACTACTGTTGTTTTTATTGTATTAGATTATGAACTCTCT
-2731 AAGGACCATTTCCGGATGGAGGATAAGAGACCATTTGATGTGGGCAGTGATGAGGCCTTCTGTTG
-2666 CACCTGGAAAGGTCAACTATATACAAGCCTGCAAGTCATTCTATAGGAGCAGGCCCCAGTGACCA
-2601 GACTCTATAGACTGTCTCCTCTTTCTGAGAGGGACAGCCATCTCTAGGTTGACTAACCTCTGAA
-2536 GCTCCTTGCAATTGGCTTTTGTGCTATGAGCCATGGATGATTCCAGACTAATCCGAGAATGCTCGT
-2471 CAAAACCCCAAGGAATTACTCAAATACTGACATAACAGACATTTTTTGAGTGGAAGAGCCGAGTTT
-2406 TTTTAAATATTCTGAAACTCATTTGTTTTTAAATGCATGAGATGGCCAAGGTCTTGCTAAGAGCT
-2341 GGCTGCAAAGCGAAAGGCAGAGAGAATGAAACCCATAGAGAGGCAGAATAACCAGAAAGGTTGG
-2276 GACTCGTTTATTTTATAATGTAAATTAGTCTATTATGAAACAATACTTGTTTACTGGTGAAAAAT

FIG. 14E

0035740.040500

-2211 TGGAAAATACAAAGAATAAAAGGAGGAAAAAATCACTCTTTAGTTTCACAAGCCAAATCAAGCC
-2146 ACTATTAAAATGGTGGTTTACTTCCTTTTATTAATTTTCTGTACATATTTTGCATAATCATGTT
-2081 GTATGTACAATTTTATGTTCTATTTTCAATATTAAGTGGTGTCTTCAAATTTCTTAATGACAA
-2016 AAATAATATATGCTCATAATAGAACATTTTAAATGCAAATAAAACAAAAATAATGTTAAAATTTA
-1951 GTAATATTTATTAATTTTCTCCAAGTGCACGAAATTACAAATGTAACAACCTAATTCCTAGTG
-1886 GCCTAATAACCCTATTTCCAGACCTCTTCTCATTACAAGGAAAACTCATATGCAGATAGTTCTA
-1821 AAGGTATGAAGTGAAAAGATAAAGATTTTCTTCCTTGCTGCATCCTCACCCCATCAGCATTATT
-1756 CCCCAGGGTAACTACTATTAATAGATAGTAATTCTACCCAAAGGAAAAATCATATGCATATAAC
-1691 AGCATCATATGTATACCTTTCTAGTAACCTACAAAACAAATGATAATATCATATCCTTTCTTATG
PvuII (-1580)
-1626 TGTATTGCTCTTTTCACTAAATGTATCTGTGATATGTGTCTATATCAGCTGATTGTCCTTTTGA
-1561 TGGCTGAATAATATTCATCTTGTCCACGTGATAGTATTACTTGACAAGCTCCCTGCTGATGGAC
-1496 ATTTGCTTTTGTACTATGATAGTAATATAATCAACATTTATATATGTTTTGTATGTATCTATAA
-1431 TACACATGCACATACACATGCATATTTCTGCAGGGATAGCCATAGTAAATAACTAGTAACGGTAT
-1366 TGCAAGTTAAAGGAACAATCTCATTGCTTGAAATTTTAAATTTTGAAATACACTGCCAATTTTCA
-1301 TGGTCTCTCCTTGTAAGCTAGTTTGGGCTTTCTCACAGCATGACAGGCTCAGGGCAGTCAGACCA
-1236 TCCTGGCCAAAGAGCAGAGTGCCACAGACCACAACCTGCTTCTAATCAGCCATCTTCCCAAAGCCT
-1171 TCTCTTTTTTCTATTAATAACTTTGTATGAGATTCCATCTTAATACTTTTCTGTGTTTGGTCTT
-1106 GTAAGAGCTTATTTTCTGAACCAGGAAGTGGTTCAGGGCGGTTTTTCTAACTTCACAGAGCTCC
-1041 CTCTTCTGTAGCTTTTGTGAAATGGTCAAAAACATAGCAGCCTGCCTTCTGAGTTCTCCATCCC
-976 ACCCTGGTTGGGCCTTCTCTATCCTTGTCTGTGTTGTTTATATCCTGCTGAAGTGTGATTCCACT

FIG. 14F

663070-8743220

-911 TGTGCAGTTTCTCCTCTGTGTAGGATCAAAGGGCTGTGGCTGGTTGGTTTGAAAATTTCTTATAC
-845 CCTAGACTATTCCAGTGCCTTTTCAAGGCTTCCAGGCCCTCTCACACTAATCTATTATCATATTG
-779 GGCAAACTCCTTGCAGTTTTCAGCTACTATTCCCTGATTGACTTTTCAGTAAATCTATCTCTCAGT
-713 CTTTCAGTATCCAAAGAAGATTGGTTCTAGGACCACCATCCCGCTGCCTCCACAGATACCAAATC
-647 AGAGGATGCTCAATTCCCTCTTATAAACGTTGCAGTATTTGCATATAATCTGCACATGTATTTCT
-581 GTATATTTTAAATCATCCCTAGATTACTTATAATACCTGATACAATATAAATGCTAAATAGCTGTA
-515 ACACTGTATCTTTAAATTTACATTATTTTTTGTTGTTGTATTATTATTTTATGTATTTTTTAA
-449 AAATATTTTCCATCTACAGTCAGTAGAATCCACGGATACAGAACCTATGGATAGGAAGGACCAACT
-383 GTATCTTTTAGTGTTTTGAGGTTCTTG

FIG. 14G

-356 AATTCTCAGGTCGTTTGCTTTCTTTGCTTTCTCCCAAGTCTTGTTTTACAATTTGCTTTAGTCA
-291 TTCACTGAAACTTTAAAAAACATTAGAAAACCTCACAGTTTGTAAATCTTTTCCCTATTATATA
-226 TATCATAAGATAGGAGCTTAAATAAAGAGTTTTAGAACTACTAAAATGTAAATGACATAGGAAA
-161 ACTGAAAGGGAGAAGTGAAAGTGGGAAATTCCTCTGAATAGAGAGAGGACCATCTCATATAAATA

CAP (-81)

-96 GGCCATACCCACGGAGAAAGGACATTCTAACTGCAACCTTTTCGAAGCCTTTGCTCTGGCACAACA

AUG (1)

-31 GGTAGTAGGGGACACTGTTCGTGTGTCAAC ATG ACC AAC AAG TGT CTC CTC CAA
25 ATT GCT CTC CTG TIG TGC TTC TCC ACT ACA GCT CTT TCC ATG AGC TAC
73 AAC TIG CTT GGA TTC CTA CAA AGA AGC AGC AAT TTT CAG TGT CAG AAG
121 CTC CTG TGG CAA TTG AAT GGG AGG CTT GAA TAC TGC CTC AAG GAC AGG

PvuII (199)

169 ATG AAC TTT GAC ATC CCT GAG GAG ATT AAG CAG CTG CAG CAG TTC CAG
217 AAG GAG GAC GCC GCA TTG ACC ATC TAT GAG ATG CTC CAG AAC ATC TTT
265 GCT ATT TTC AGA CAA GAT TCA TCT AGC ACT GGC TGG AAT GAG ACT ATT
313 GTT GAG AAC CTC CTG GCT AAT GTC TAT CAT CAG ATA AAC CAT CTG AAG
361 ACA GTC CTG GAA GAA AAA CTG GAG AAA GAA GAT TTC ACC AGG GGA AAA
409 CTC ATG AGC AGT CTG CAC CTG AAA AGA TAT TAT GGG AGG ATT CTG CAT
457 TAC CTG AAG GCC AAG GAG TAC AGT CAC TGT GCC TGG ACC ATA GTC AGA
505 GTG GAA ATC CTA AGG AAC TTT TAC TTC ATT AAC AGA CTT ACA GGT TAC

BglII (565)

553 CTC CGA AAC TGAAGATCTCCTAGCCTGTGCCTCTGGGACTGGACAATTGCTTCAAGCATTCT
615 TCAACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCATATGAAAGGACACTAGAAG

FIG. 15A

680 ATTTTGAAATTTTTATTAAATTATGAGTTATTTTTATTTATTTTAAATTTTATTTTGGAAAATAAA
745 TTATTTTTTGGTGCAAAGTCAACATGGCAGTTTTAATTTTCGATTTGATTTATATAACCATCCATA
810 TTATAAAATTGCCAAGTACCTATTAGTTGTTCTTTTTTAAATATACCTGCAAAGTAGTATACTTT
875 CTGGCCCCCTGCCTTTAAGGAATTTAAAATTCAAGAAAGCCATGATGGAATATATAAGGTAAGAGA
940 CAATAAGGGGACCTGAACCTTATGGGGGAATAAATATGGCATGAACTGCTGTGGGATTAAAGAG
1005 AAAAGGAAAGCTGGAGGGTCTGGAACTAAACCTGGGGTTC CATTCCTCCTACTGTGTGTTCCAG
Ball (1099)
1070 ATTCTCTCATCATAAAGTTAGAATTGAGCTGGCCATCAGGAATAGCCAGAGGAATATGTCAGCTT
1135 TTGTGTTCTCCCTAACCTTCCCCAGTTATTTGGGGGATCACTTTGCTCCTCGAAAGATTTTTTAA
1200 TAATTATGTGCCCCCACCATCCCTGCAA

Ball (1099)

1135 TTGTGTTCTCCCTAACCTTCCCCAGTTATTTGGGGGATCACTTTGCTCCTCGAAAGATTTTATAA

FIG. 15B

Activation of the Human β -interferon Gene by Homologous Recombination with pINT β -1

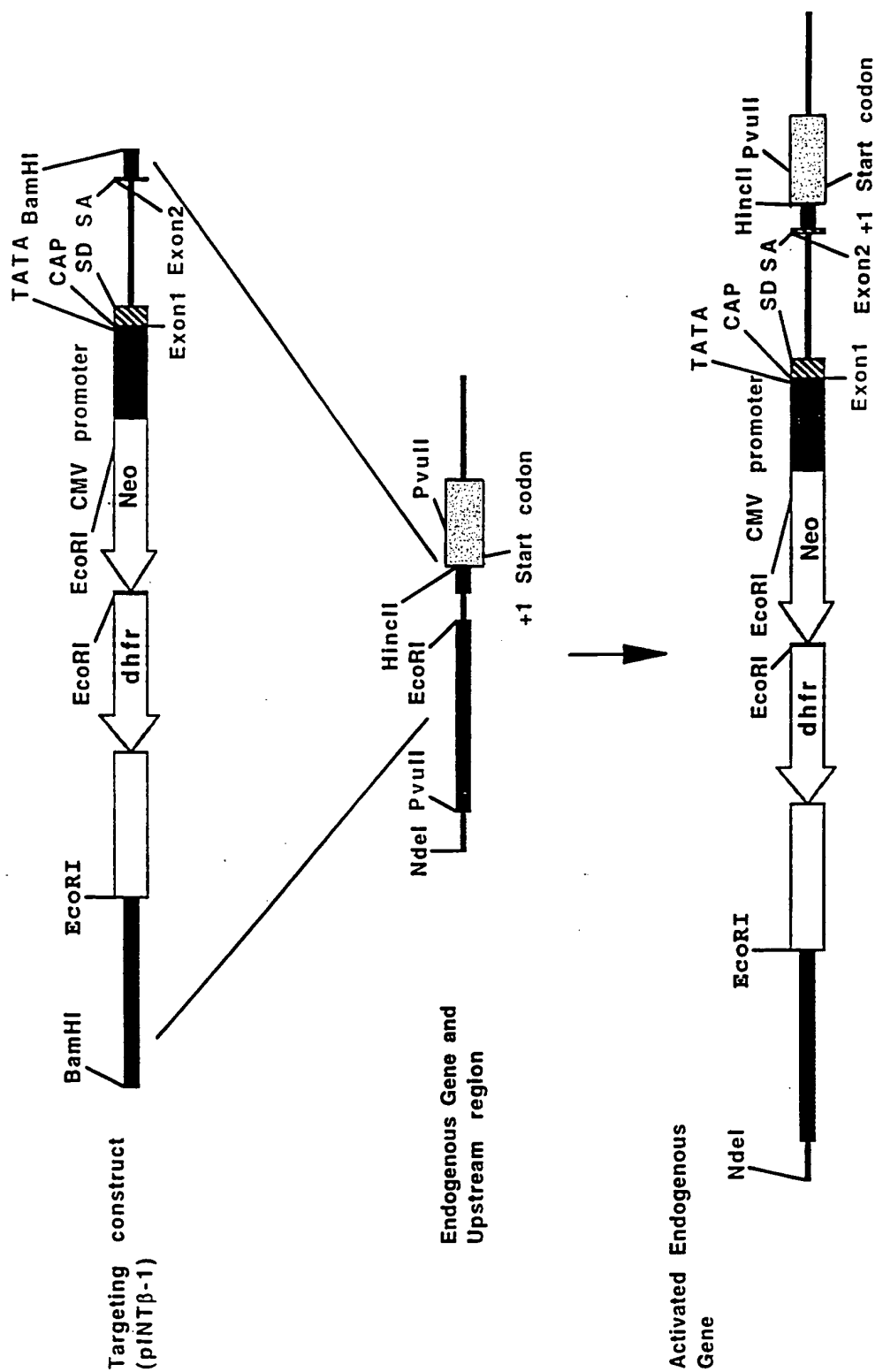


FIG. 16